AMENDMENTS TO THE SPECIFICATION:

On page 3, please replace the paragraph beginning at line 3 with the following amended paragraph:

Methods and compositions that have been used to target and alter, by homologous recombination, substitutions, insertions and deletions in target sequences have been described; see U.S. application serial nos. 08/381,634 (abandoned); 08/882,756 (now U.S. Patent No. 5,929,043); 09/301,153 (now U.S. Patent No. 6,245,565); 08/781,329 (now U.S. Patent No. 5,989,879); 09/288,586 (now U.S. Patent No. 6,200,812); 09/209,676 (now U.S. Patent No. 6,524,856); 09/007,020 (now U.S. Patent No. 6,090,539); 09/179,916 (now U.S. Patent No. 6,391,564); 09/182,102; 09/182,097 (now abandoned); 09/181,027; 09/260,624; and ~~internation~~ international application nos. US97/19324 (WO 98/17827); US98/26498 (WO 99/37755); US98/01825 (WO 98/34118).

On page 15, please replace the paragraph beginning at line 19 with the following amended paragraph:

In a preferred embodiment, two substantially complementary single-stranded targeting polynucleotides are used. The two complementary single-stranded targeting polynucleotides are usually of equal length, although this is not required. However, as noted below, the stability of the four strand hybrids of the invention is putatively related, in part, to the lack of significant unhybridized single-stranded nucleic acid, and thus significant unpaired sequences are not preferred. Furthermore, as noted above, the complementarity between the two targeting polynucleotides need not be perfect. The two complementary single-stranded targeting polynucleotides are simultaneously or contemporaneously introduced into a target cell harboring a predetermined endogenous target sequence, generally with at lease one recombinase protein (e.g., RecA). Under most circumstances, it is preferred that the targeting polynucleotides are incubated with RecA or other recombinase prior to introduction into a target cell, so that the recombinase protein(s) may be "loaded" onto the targeting polynucleotide(s), to coat the nucleic acid, as is described below. Incubation conditions for such recombinase loading are described infra, and also in U.S.S.N. 07/755,462, filed 4 September 1991 (now U.S. Patent No. 5,273,881); U.S.S.N. 07/910,791, filed 9 July 1992; and U.S.S.N. 07/520,321, filed 7 May 1990 (now U.S.

Patent No. 5,223,414), each of which is incorporated herein by reference. A targeting polynucleotide may contain a sequence that enhances the loading process of a recombinase, for example a RecA loading sequence is the recombinogenic nucleation sequence poly[d(A-C)], and its complement, poly[d(G-T)]. The duplex sequence poly[d(A-C)•d(G-T)$_n$, where n is from 5 to 25, is a middle repetitive element in target DNA.

On page 16, please replace the paragraph beginning at line 19 and continuing onto page 17, line 4, with the following amended paragraph:

In addition, when the targeting polynucleotides are used to generate insertions or deletions in an endogenous nucleic acid sequence, as is described herein, the use of two complementary single-stranded targeting polynucleotides allows the use of internal homology clamps as depicted in the figures of PCT US98/05223 (WO 98/42727). The use of internal homology clamps allows the formation of stable deproteinized cssDNA:probe target hybrids with homologous DNA sequences containing either relatively small or large insertions and deletions within a homologous DNA target. Without being bound by theory, it appears that these probe:target hybrids, with heterologous inserts in the cssDNA probe, are stabilized by the re-annealing of cssDNA probes to each other within the double-D-loop hybrid, forming a novel DNA structure with an internal homology clamp. Similarly stable double-D-loop hybrids formed at internal sites with heterologous inserts in the linear DNA targets (with respect to the cssDNA probe) are equally stable. Because cssDNA probes are kinetically trapped within the duplex target, the multi-stranded DNA intermediates of homologous DNA pairing are stabilized and strand exchange is facilitated.

On page 23, please replace the paragraph beginning at line 10 with the following amended paragraph:

In a preferred embodiment, the targeting polynucleotides are coated with recombinase prior to introduction to the domain target. The conditions used to coat targeting polynucleotides with recombinases such as RecA protein and ATPγS have been described in commonly assigned U.S.S.N. 07/910,791, filed 9 July 1992; U.S.S.N. 07/755,462, filed 4 September 1991; and U.S.S.N. 07/520,321, filed 7 May 1990, and PCT US98/05223 (WO 98/42727), each incorporated herein by reference. The procedures below are directed to the use of E. coli RecA,

although as will be appreciated by those in the art, other recombinases may be used as well. Targeting polynucleotides can be coated using GTPγS, mixes of ATPγS with rATP, rGTP and/or dATP, or dATP or rATP alone in the presence of an rATP generating system (Boehringer Mannheim). Various mixtures of GTPγS, ATPγS, ATP, ADP, dATP and/or rATP or other nucleosides may be used, particularly preferred are mixes of ATPγS and ATP or ATPγS and ADP.

On page 23, please replace the paragraph beginning at line 21 with the following amended paragraph:

RecA protein coating of targeting polynucleotides is typically carried out as described in U.S.S.N. 07/910,791, filed 9 July 1992 and U.S.S.N. 07/755,462, filed 4 September 1991, and PCT US98/05223 (WO 98/42727), which are incorporated herein by reference. Briefly, the targeting polynucleotide, whether double-stranded or single-stranded, is denatured by heating in an aqueous solution at 95-100°C for five minutes, then placed in an ice bath for 20 seconds to about one minute followed by centrifugation at 0°C for approximately 20 sec, before use. When denatured targeting polynucleotides are not placed in a freezer at -20°C they are usually immediately added to standard RecA coating reaction buffer containing ATPγS, at room temperature, and to this is added the RecA protein. Alternatively, RecA protein may be included with the buffer components and ATPγS before the polynucleotides are added.